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WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
A61B 5/04, 17/36, A61F 2/00, 7/00

A1

(11) International Publication Number: WO 98/30144

(43) International Publication Date: 16 July 1998 (16.07.98)

(21) International Application Number: PCT/IL97/00307

(22) International Filing Date: 15 September 1997 (15.09.97)

(30) Priority Data:
PCT/IL97/00011 8 January 1997 (08.01.97) WO
(34) Countries for which the regional or international application was filed: IL et al.

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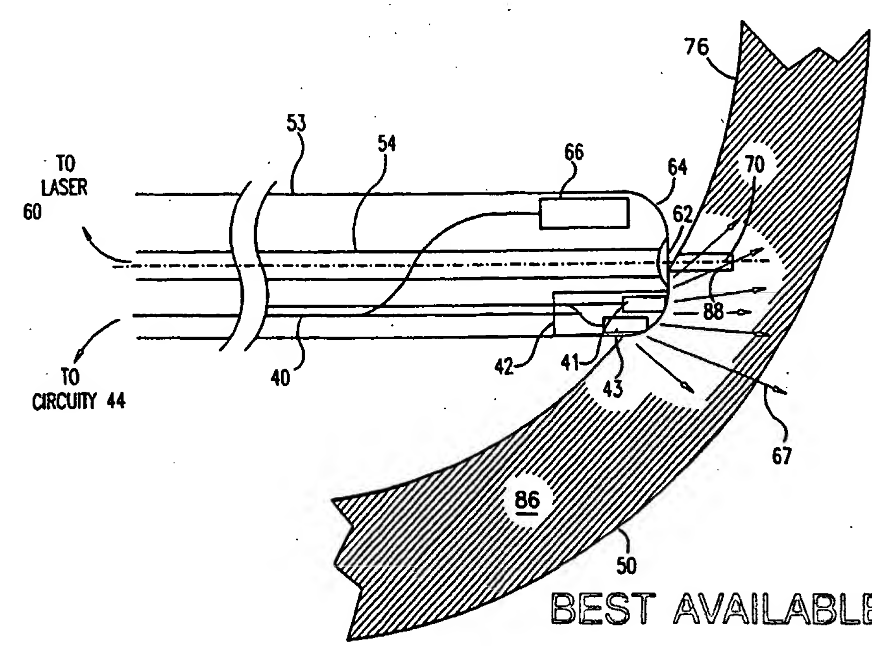
(81) Designated States: AL, AM, AT, AT (Utility model), AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ (Utility model), DE, DE (Utility model), DK, DK (Utility model), EE, EE (Utility model), ES, FI, FI (Utility model), GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK (Utility model), SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: MONITORING OF MYOCARDIAL REVASCULARIZATION



(57) Abstract

This invention is an apparatus for PMR treatment, including an elongate probe (52) having a distal end (64) for engaging heart tissue (86) of a subject, and a revascularization device (60) which imparts energy to the heart tissue (86) for generating perfusion enhancing channels therein. A sensor (42) provides an indication responsive to the treatment, preferably by receiving signals generated by the body of the subject.

MONITORING OF MYOCARDIAL REVASCULARIZATION

RELATED APPLICATION

This application is a continuation-in-part of PCT patent application no. PCT/IL97/00011, filed January 8, 1997, which is incorporated herein by reference.

FIELD OF THE INVENTION

The present invention relates generally to methods and devices for cardiac surgery, and specifically to methods and apparatus for myocardial revascularization.

BACKGROUND OF THE INVENTION

Myocardial revascularization is a technique, known in the art, for creating channels in ischemic heart tissue to improve the blood supply to ischemic myocardium. It may be performed by various techniques, the best-known of which is laser myocardial revascularization, which employs laser radiation for generating such channels.

In transmyocardial revascularization (TMR), as is known in the art, a computer-controlled laser is used to drill penetrating holes about 1 mm in diameter in the myocardium by delivering laser energy to the epicardium through an incision in the chest and the pericardium. Blood at the outer, epicardial openings of the channels typically clots after a few minutes, but the inner portions of the channels, communicating with the ventricle, remain patent. It is hypothesized that during systole, blood flows through these channels into naturally-existing myocardial sinusoids, supplementing the impaired arterial blood supply.

According to another hypothesis, the local injury caused to the myocardium by various forms of energy (e.g., laser radiation, as described above, or alternatively, RF radiation, or ultrasonic or mechanical energy) stimulates local angiogenesis, eventually supplementing the impaired arterial blood supply. Although there are no conclusive answers at present regarding the underlying mechanism, there is clinical evidence of the treatment's therapeutic efficacy.

U.S. patent 5,389,096, to Aita, et al., which is incorporated herein by reference, describes methods and apparatus for percutaneous myocardial revascularization (PMR). A deflectable, elongated lasing apparatus is guided to an area within the patient's heart, and the distal end of the apparatus is directed to an area of interest in the inner wall of the heart. The wall is irradiated with laser energy to form channels therein, preferably without perforating the epicardium. Alternatively, PMR may be carried out by applying other energy forms, as described above, from inside the art.

In TMR, as is known in the art, the channels are created through the myocardium from the outside in, and the transient blood stream ensuing upon channel completion constitutes an intrinsic indication of successful drilling. In PMR, however, the channel is generated from inside the heart chamber and, preferably, does not penetrate the myocardium. Consequently there is no direct indication of successful generation of the channel.

waves to resolve zones of differing tissue characteristics, in particular density, thus imaging the channels' dimensions and direction.

Other aspects of the present invention use real-time sensing technologies, particularly based on optical sensing, for detecting local changes in blood perfusion. By comparing pre- and post-PMR optical signals, enhanced blood perfusion of ischemic zones, due to successful channel generation, may be observed.

Some preferred embodiments of the present invention are based on a PMR catheter as described in PCT patent application no. PCT/IL97/00011, filed January 14, 1997, which is assigned to the assignee of the present patent application, and whose disclosure is incorporated herein by reference. The catheter comprises a waveguide, for conveying energy to the endocardium, preferably laser energy, and has at least one sensor at its distal tip. The sensor may comprise one or more electrophysiological sensing electrodes, position sensors, ultrasound transducers, or other sensors known in the art.

In some of these preferred embodiments, the sensor comprises an electrode, which receives electrical signals from the heart indicative of the efficacy of local PMR treatment, i.e., whether an energy pulse or series of pulses has actually succeeded in generating a channel of substantial depth in the myocardium. The catheter is coupled to signal processing circuitry, which processes the signals received by the electrode and provides an indication to a user of the catheter, typically an interventional cardiologist, as to whether the channel has been generated. The indication is typically based on elevation of the ST segment and/or VPB's in the local electrogram during at least several minutes after the channel has been generated. Failure to sense such a change after one or several energy pulses is taken to be an indication of an error or malfunction, requiring the cardiologist's intervention. Preferably, the catheter is held in place at a candidate site for a period both before and after channel generation, long enough to gather pre- and post-PMR electrograms, which are compared to ascertain the efficacy of the local treatment.

Preferably, the elevated ST effect, which is of a highly localized nature and significantly long duration, also provides an indication to the user during subsequent PMR channel generation as to whether a channel preexists in a new candidate area.

In some of these preferred embodiments, the electrode is used for gating the energy source, as described in PCT patent application no. PCT/IL97/00011, mentioned above, as well as sensing signals indicative of successful channel generation.

In some preferred embodiments of the present invention, ECG is measured during the PMR procedure by means of skin electrodes. Disturbances of the normal sinus rhythm, particularly ventricular premature beats (VPB's), are sensed as an indication that an energy pulse has successfully generated a channel in the myocardium. Absence of such disturbance is, similarly, taken to indicate error or malfunction.

In other preferred embodiments of the present invention, the sensor at the distal end of the catheter comprises an ultrasonic transducer. The transducer generates signals responsive to

Preferably, the sensor receives signals generated by the body of the subject responsive to the treatment.

Further preferably, the sensor includes an electrode, which is positioned on the probe adjacent the distal end thereof.

Alternatively or additionally, the electrode is placed on the subject's body independently of the probe.

In preferred embodiments, the sensor includes a transducer, preferably an ultrasonic transducer, which generates signals indicative of the treatment.

Alternatively or additionally, the sensor includes a blood flow sensor, which generates signals responsive to microcirculation.

Preferably, the transducer is positioned on the probe adjacent the distal end thereof.

In another preferred embodiment, the sensor includes an optical sensor, and the apparatus preferably includes a waveguide, which transmits fluorescence-stimulating radiation to the myocardial tissue, wherein the sensor receives fluorescence emitted from the tissue and generates signals indicative of the treatment.

Preferably the apparatus includes signal processing circuitry, which is coupled to the sensor and analyzes the signals to provide an indication of the efficacy of the treatment. Preferably, the circuitry detects an elevated ST segment or, alternatively or additionally, an arrhythmia. Preferably, the arrhythmia detected by the circuitry includes at least one VPB.

Alternatively or additionally, the circuitry detects a change in tissue characteristics adjacent to the distal end of the probe. Preferably, the change includes a change in tissue density, or, alternatively or additionally, an increase in blood perfusion adjacent to the distal end of the probe.

Preferably, the revascularization device applies laser radiation to the heart tissue.

Alternatively, the revascularization device applies RF energy, high-intensity ultrasonic radiation, and/or mechanical energy to the heart tissue.

There is also provided, in accordance with a preferred embodiment of the present invention, a method for monitored PMR treatment of the heart of a subject, including:

bringing a probe, including a revascularization device for imparting energy to the heart, into engagement with heart tissue of a subject;

imparting energy to the heart tissue using the device so as to generate perfusion-enhancing channels therein; and

receiving a signal from the body of the subject responsive to the treatment.

Preferably, receiving the signal includes receiving a signal generated by the body of the subject indicative of successful performance of the treatment.

Further preferably, sensing the signal includes sensing an electrical signal inside the heart of the subject, or,

alternatively or additionally, on a surface of the body of the subject.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1A is a schematic illustration showing electrical signals received from the body of a subject before, during and after PMR laser firing;

Fig. 1B is a schematic illustration showing the signals of Fig. 1A on an expanded time scale;

Fig. 2A is a schematic illustration of a catheter system for use in PMR, in accordance with a preferred embodiment of the present invention;

Fig. 2B is a schematic illustration showing details of the distal end of the catheter of Fig. 2A, in accordance with a preferred embodiment of the present invention;

Fig. 3A is a schematic, sectional illustration of a human heart, into which the catheter of Figs. 2A and 2B is inserted for performing a PMR procedure therein, in accordance with a preferred embodiment of the present invention;

Fig. 3B is a schematic, sectional detail illustration showing a channel drilled in the tissue of the heart of Fig. 3A, in accordance with a preferred embodiment of the present invention;

Fig. 4 is a schematic illustration showing details of the distal end of a catheter for PMR, in accordance with an alternative preferred embodiment of the present invention;

Fig. 5 is a schematic illustration of a human body and heart, into which the catheter of Figs. 2A and 2B is inserted to perform a PMR procedure therein, in accordance with another preferred embodiment of the present invention;

Fig. 6 is a flowchart illustrating a method of monitored PMR, in accordance with a preferred embodiment of the present invention;

Fig. 7A is a schematic illustration showing details of the distal end of a catheter for PMR, in accordance with an alternative preferred embodiment of the present invention; and

Fig. 7B is a schematic illustration showing details of the distal end of a catheter for PMR, in accordance with yet another preferred embodiment of the present invention.

the catheter, typically an interventional cardiologist, as to whether the channel has been generated.

Additionally or alternatively, the signal processing circuitry analyzes the data and gives the user a "go/no go" indication as to whether the channel has been successfully generated.

Catheter 52 preferably also includes a position sensor 66, fixed in a known position adjacent distal end 64, for use in navigating and positioning the catheter within the heart, as described more fully in PCT patent application no. PCT/IL97/00011, incorporated herein by reference.

As shown in Fig. 2B, catheter 52 includes a sensor unit 42 at its distal end 64. Preferably, sensor unit 42 comprises an electrode 43 for sensing electrical potentials in heart tissue adjacent to distal end 64. Local electrogram signals from electrode 43 are conveyed by wires 40 to circuitry 44. Preferably, these signals are used to monitor the changes in the electrogram signals due to the PMR drilling, as described above, thus indicating successful channel drilling. The electrogram signals may also be used to trigger laser source 60, as disclosed in PCT patent application no. PCT/IL97/00011, mentioned above.

Although catheter system 50 is shown and described with reference to electrode 43, it will be understood that sensor unit 42 may include other sensors and other types of elements. For example, additional electrodes may be placed at or adjacent to distal end 64, either on catheter 52 itself or on a structure fixed to the catheter, as described in PCT patent application no. PCT/IL97/00009, filed January 8, 1997, which is assigned to the assignee of the present patent application, and whose disclosure is incorporated herein by reference.

Fig. 3A is a schematic, sectional illustration showing catheter 52 inserted into heart 70 of a subject, in accordance with a preferred embodiment of the present invention. Catheter 52 is fed percutaneously into the subject's vascular system, for example, through the femoral artery, and is passed through aorta 72 into left ventricle 74 of heart 70. Distal end 64 is positioned against endocardium 76 in a desired position and orientation and drills channels therein, preferably, as described in the above-mentioned PCT patent application no. PCT/IL97/00011.

Fig. 3B is a schematic, sectional illustration showing details of catheter 52 drilling a channel 88 in myocardium 86 of heart 70, in accordance with a preferred embodiment of the present invention. Electrode 43 measures the local electrical signals prior to, during and after the drilling to assess successful drilling, as described above.

Fig. 4 is a schematic illustration showing details of another catheter 53 for use in PMR, in accordance with alternative preferred embodiments of the present invention. Catheter 53 includes waveguide 54, lens 62 and position sensor 66, and is coupled to console 58, substantially as described above with reference to catheter 52. Additionally, sensor unit 42 of catheter 53 includes an ultrasound transducer 41. Preferably, transducer 41 comprises a transducer array, as is known in the art, which emits a beam 67 that may be steered over a range

below with reference to catheter 52, shown in Figs. 2A and 2B, but it will be understood that the principles of this method may be applied using other suitable catheters, as described hereinabove.

Prior to beginning PMR, at least one candidate area for the procedure is identified within heart 70, preferably as described in the above-mentioned PCT patent application no. PCT/IL97/00011.

Catheter 52 is then navigated to the candidate area. The position and orientation of distal end 64 of the catheter are preferably ascertained and controlled by receiving signals from position sensor 66, and are compared with a stored map of the heart, although such position and orientation sensing are not a necessary part of the present invention. When the distal end is suitably positioned and oriented, intracardiac electrogram signals are received and stored by console 48. Laser source 60 is fired to drill a channel in the heart tissue, as described above. Following the laser firing, post-PMR readings are taken by electrode 43 and analyzed, preferably by comparing them with the pre-PMR signals, for indication of successful drilling. The position of the channel is marked on the map, and catheter 52 is then repositioned to drill the next channel. This procedure is preferably repeated until channels have been drilled to a desired density over the entire candidate area.

It will be understood that as described above, the method of monitored PMR shown in Fig. 6 may similarly be implemented by monitoring the skin surface ECG or by using ultrasound or other sensing modalities. Similarly, the PMR procedure may be carried out using other methods of PMR, such as RF or mechanical methods, mentioned above, in place of the laser.

Reference is now made to Fig. 7A, which is a schematic illustration showing details of a catheter 90 for use in monitored PMR, in accordance with an alternative preferred embodiment of the present invention. Catheter 90 includes waveguide 54, lens 62 and position sensor 66, and is coupled to console 58, substantially as described above with reference to catheter 52. Additionally, sensor unit 42 of catheter 90 includes a blood flow sensor 92, which senses signals responsive to blood flow within microvasculature 94 in a vicinity of channel 88, generated by the catheter.

Sensor 92 preferably comprises an optical detector, which senses microperfusion and/or tissue oxygenation based on light reflected from the heart tissue. For example, the sensor may be used to detect NADH activity, as described in the above-mentioned articles by Kedem, Furman and Duboc, or to detect the concentration of a contrast agent or fluorescent marker. Alternatively, sensor 92 may comprise an ultrasound transducer. Sensor 92 is coupled via wires 40 to circuitry 44.

When catheter 90 is brought into contact with endocardium 76, sensor 92 receives signals from the vicinity of channel 88. Signals prior to and after the PMR procedure are compared, so as to detect changes in local blood flow in the vicinity. An enhancement of the local blood flow following the procedure, indicated by increased microperfusion and/or tissue oxygenation, is generally a sign of successful channel generation.

CLAIMS

1. Apparatus for PMR treatment, comprising:

an elongate probe having a distal end for engaging heart tissue of a subject, and comprising a revascularization device, which imparts energy to the heart tissue for generating perfusion-enhancing channels therein; and

a sensor, which provides an indication responsive to the treatment.

2. Apparatus according to claim 1, wherein the sensor receives signals generated by the body of the subject responsive to the treatment.

3. Apparatus according to claim 2, wherein the sensor comprises an electrode.

4. Apparatus according to claim 3, wherein the electrode is positioned on the probe adjacent the distal end thereof.

5. Apparatus according to claim 3, wherein the electrode is placed on the subject's body independently of the probe.

6. Apparatus according to claim 1, wherein the sensor comprises a transducer which generates signals indicative of the treatment.

7. Apparatus according to claim 6, wherein the transducer comprises an ultrasonic transducer.

8. Apparatus according to claim 6, wherein the transducer is positioned on the probe adjacent the distal end thereof.

9. Apparatus according to claim 1, wherein the sensor comprises a blood flow sensor, which generates signals responsive to microcirculation.

10. Apparatus according to claim 1, wherein the sensor comprises an optical sensor.

21. Apparatus according to any of claims 1-11, wherein the revascularization device applies high-intensity ultrasonic radiation to the heart tissue.

22. Apparatus according to any of claims 1-11, wherein the revascularization device applies mechanical energy to the heart tissue.

23. A method for monitored PMR treatment of the heart of a subject, comprising:

bringing a probe, including a revascularization device for imparting energy to the heart, into engagement with heart tissue of a subject;

imparting energy to the heart tissue using the device so as to generate perfusion-enhancing channels therein; and

receiving a signal from the body of the subject responsive to the treatment.

24. A method according to claim 23, wherein receiving the signal comprises receiving a signal indicative of successful performance of the treatment.

25. A method according to claim 23, wherein receiving the signal comprises sensing a signal generated by the body of the subject.

26. A method according to claim 25, wherein sensing the signal comprises sensing an electrical signal inside the heart of the subject.

27. A method according to claim 25, wherein sensing the signal comprises sensing an electrical signal on a surface of the body of the subject.

28. A method according to claim 23, wherein receiving the signal comprises receiving energy reflected from the heart tissue.

29. A method according to claim 28, wherein receiving energy comprises receiving ultrasonic energy from a designated channel location within the heart.

40. A method according to claim 38, wherein detecting the change comprises detecting a change in blood perfusion in the tissue.

41. A method according to claim 40, wherein detecting the change in blood perfusion comprises detecting an enhancement of the perfusion.

42. A method according to any of claims 23-33, wherein imparting energy to the heart comprises imparting laser radiation.

43. A method according to any of claims 23-33, wherein imparting energy to the heart comprises imparting RF radiation.

44. A method according to any of claims 23-33, wherein imparting energy to the heart comprises imparting high-intensity ultrasonic radiation.

45. A method according to any of claims 23-33, wherein imparting energy to the heart comprises imparting mechanical energy.

FIG. 1B

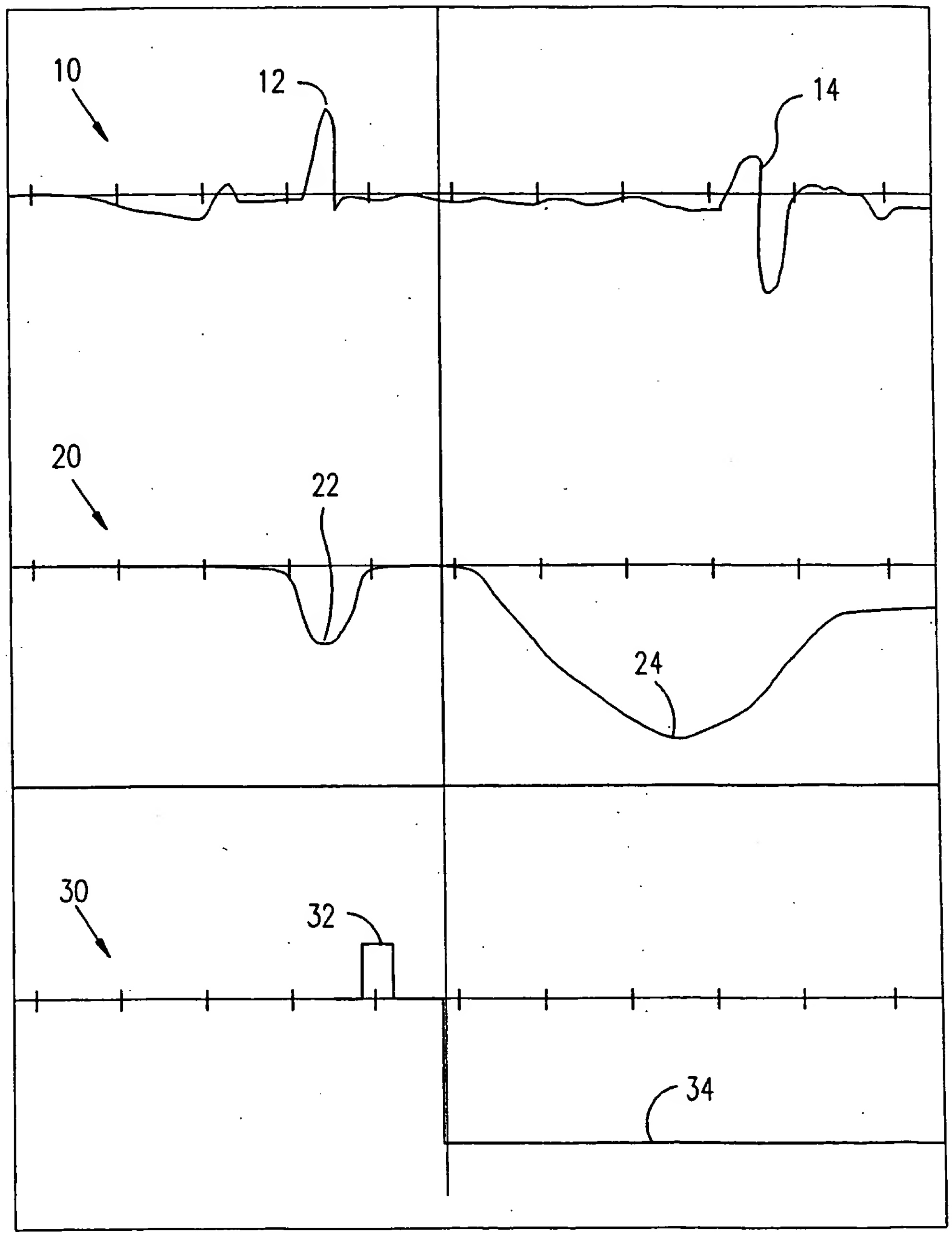


FIG. 2B

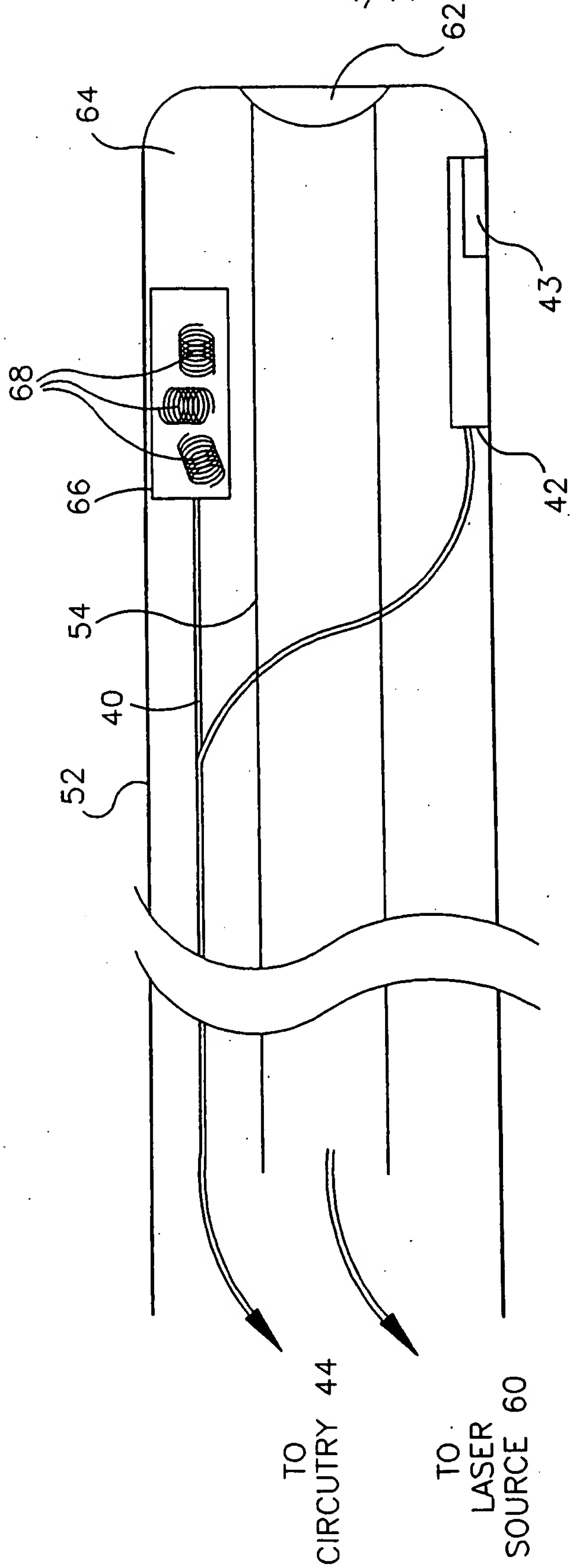
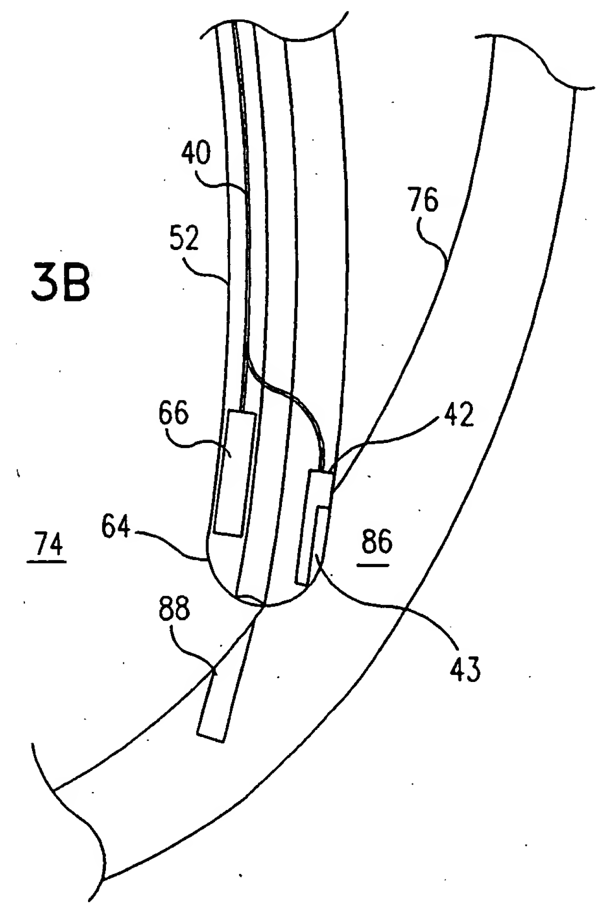


FIG. 3B



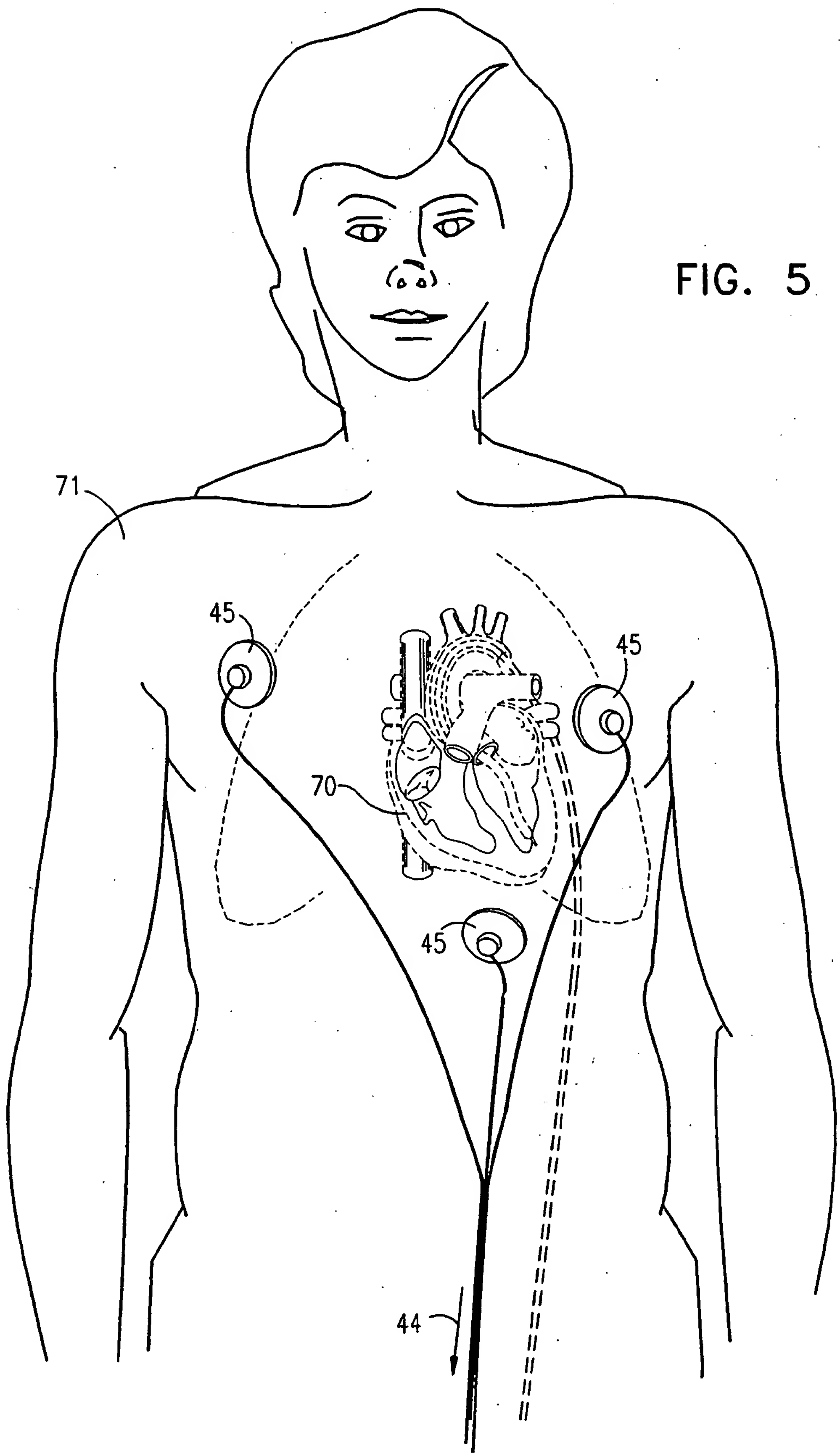


FIG. 5

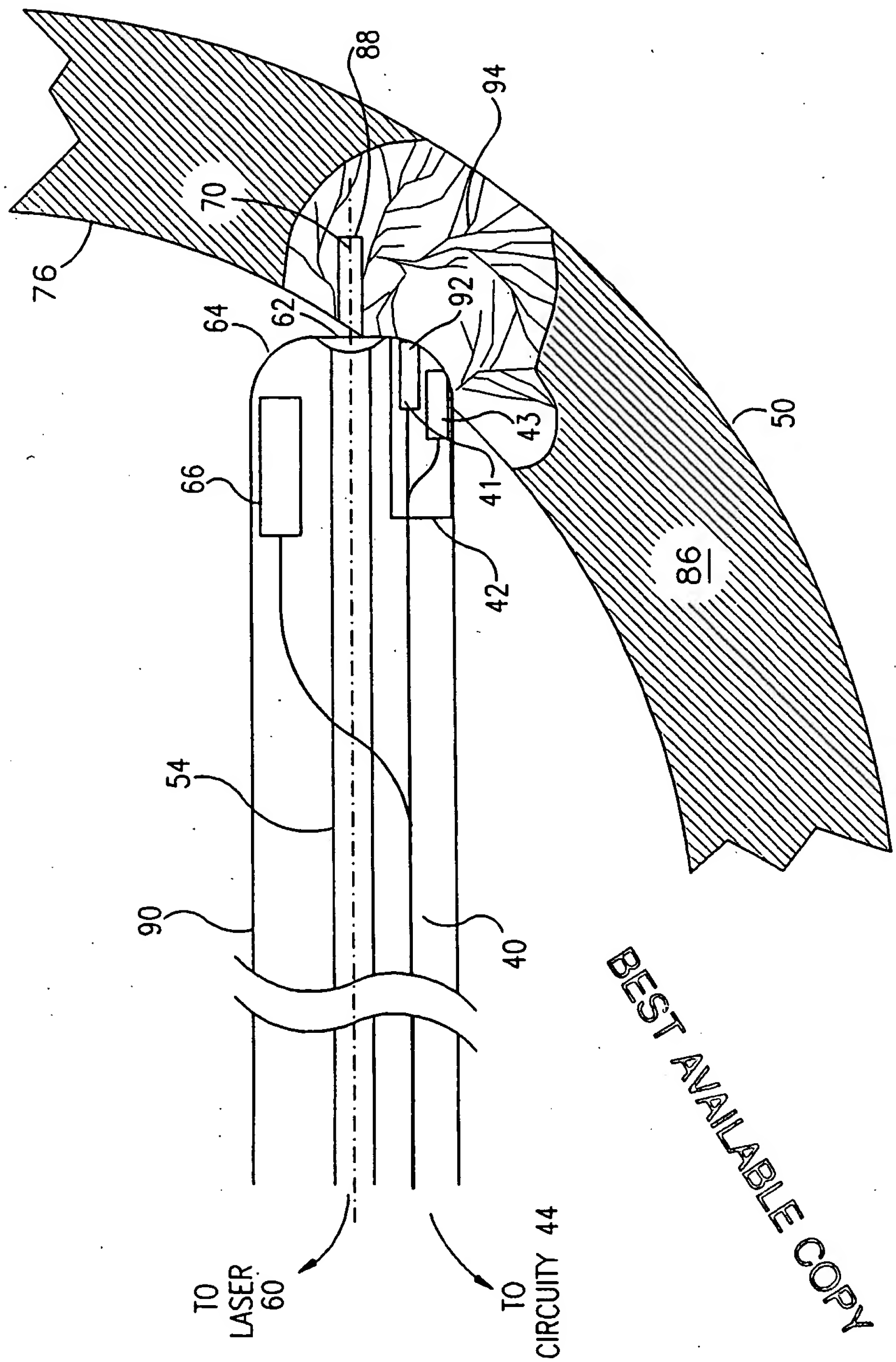

88
94
70
76
64
62
92
43
41
66
42
86
50
54
90
40
TO LASER 60
TO CIRCUITY 44

FIG. 7A

INTERNATIONAL SEARCH REPORT	International application No. PCT/IL97/00307

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61B 5/04, 17/36; A61F 2/00, 7/00
US CL :600/515, 517; 606/14, 607/98, 100, 101
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 600/438, 466, 467, 508, 515, 517; 606/2, 3, 7, 11, 12, 14-18; 607/89, 98-102, 122

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,389,096 A (AITA et al) 14 February 1995, entire document.	1 19-23, 42-45
Y	US 5,350,375 A (DECKELBAUM et al.) 27 September 1994, entire document.	1, 2, 6, 10-12, 23-25, 28, 30-32, 34, 38, 39
A,P	US 5,620,439 A (ABELA et al.) 15 April 1997, entire document.	1, 23
A,T	US 5,607,421 A (JEEVAVANDAM et al) 04 March 1997, entire document.	1, 23

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date		
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed	"&"	document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 DECEMBER 1997	08 JAN 1998

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Fluorescence lifetime-based imaging and spectroscopy in tissues and other random media

Patent number: CN1200174
Publication date: 1998-11-25
Inventor: SEVICK-MURACA E M (US); PAITHANKAR D Y (US)
Applicant: PURDUE RESEARCH FOUNDATION (US)
Classification:
- international: G01N21/64
- european:
Application number: CN19960197632 19960823
Priority number(s): US19950002746P 19950824

Also published as:

WO9708538 (A1)
EP0846262 (A1)
EP0846262 (A4)

Abstract not available for CN1200174
Abstract of correspondent: **WO9708538**

A system and method non-invasive biomedical optical imaging and spectroscopy with low-level light is described. The technique consists of a modulated light source (120) coupled to tissue (100) of a patient to introduce excitation light. Fluorescent light emitted in response to the excitation light is detected with sensor (148). The AC intensity and phase of the excitation and detected fluorescent light is provided to a processor (160) operatively coupled to sensor (148). Processor (160) employs the measured re-emission kinetics of excitation and fluorescent light to "map" the spatial variation of one or more fluorescence characteristics of the tissue (100). The fluorescence characteristic may be provided by exogenous contract agents, endogenous fluorophores, or both. The variations is determined by solving frequency domain diffusion equations at a number of designated points in the tissue as part of a recursive estimation algorithm. Processor (160) generates an imaging signal in accordance with the spatial variation of the fluorescence characteristic for provision to an output device (164). The output device (164) displays an image corresponding spatial variation of the fluorescence characteristic which corresponds to tissue (100) to aid in the detection and diagnosis of disease.